Role of the Pulmonary Vein in the Genesis of Atrial Fibrillation: Insights from a Biophysically Detailed Computational Model

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, as well as the major cause of stroke. Several lines of evidence point to a particularly important role of the left atrium (LA) in maintaining AF. Primarily, it has been suggested that "driver" regions within the LA, which act as high-frequency excitation sources during AF, are localized around sleeves of the pulmonary vein (PV). However, mechanisms by which latently pacemaking cells of the PV can initiate/maintain AF are unclear. We study such mechanisms using a biophysically detailed 3D tissue model of rabbit atria. Single-cell action potential (AP) models for rabbit atrial cells have been developed previously, which include left and right atrial (LA and RA) cells, cells of the RA bundles of the crista terminalis (CT) and pectinate muscles (PM), cells forming two major inter-atrial connections through the Bachmann's bundle (BB) and coronary sinus (CS), and pacemaking cells of the PV. All cell models were incorporated into a caricature 3D geometry comprising square LA and RA tissues, two intra- (CT and PM) and two inter-atrial (BB and CS) conductive bundles and a cylindrical PV entering the LA (Fig. 1).

Results

The 3D model was used to simulate several excitation wave patterns within the atria: (1) propagation of normal periodic APs onto the PV; (2) emergence of an ectopic wave source due to spontaneous AP firing within the PV; (3) interaction of reentrant spiral waves with the PV. Interaction of periodic plane waves simulating slow heart rhythm with "ectopic" APs generated within the PV (Figs. 1, 2) led to wave break-down and development of reentrant spirals (Figs. 3, 4). However, spiral waves originated elsewhere within the RA and LA could not be pinned to the PV for physiologically relevant values of the PV parameters (Fig. 5). Besides, the intrinsically slow ectopic source in the PV (firing rate ~1 Hz) was suppressed by either rotating spirals (Fig. 5) or periodic waves during the fast "normal rhythm" (Fig. 6). Hence, the PV may not be responsible for maintaining the high-frequency reentrant sources during AF (~10 Hz). In summary, our 3D atrial tissue model provides mechanistic insights into the role of the PV in the genesis of AF, primarily conditions for the initiation of ectopic APs breaking down the normal periodic waves, and the development of a fibrillatory state.

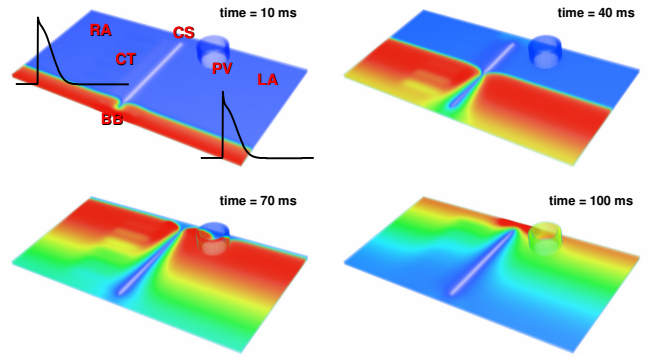

Figure 1. Initiation and propagation of APs through the RA and LA towards the PV.

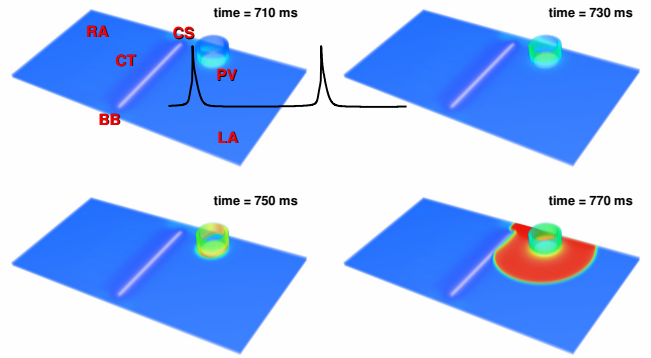

Figure 2. Initiation and propagation of an "ectopic" AP from the PV through the LA.

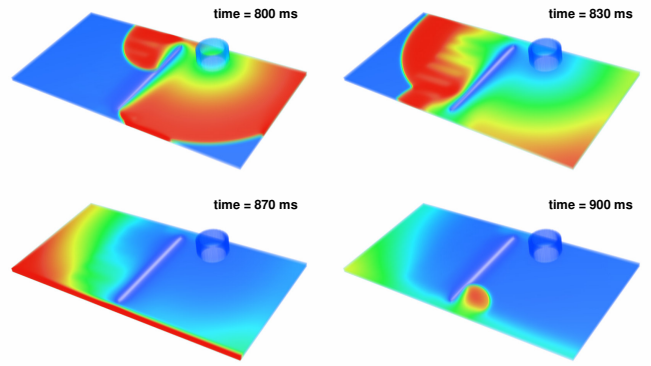

Figure 3. Interaction of the "ectopic" propagating AP with a "normal" plane wave.

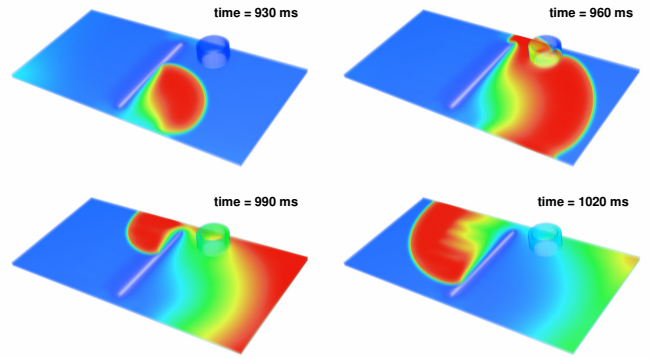

Figure 4. Initiation and propagation of a reentrant spiral wave within the RA and LA.

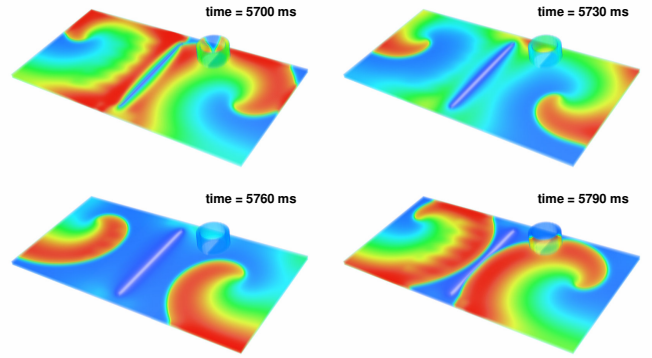

Figure 5. Spiral waves rotating within the RA and LA are not "pinned" to the PV.

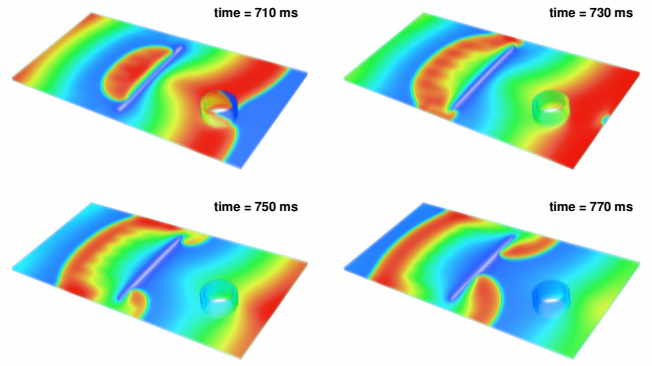

Figure 6. Fast periodic pacing ("normal rhythm") suppresses ectopics in the PV.

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